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## Unexpected C<sub>carbene</sub>-X (X: I, Br, Cl) Reductive Elimination From N-Heterocyclic Carbene Copper Halide Complexes Under Oxidative Conditions

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### Abstract

The non-innocent behaviors of NHC ligands have attracted wide attention due to their important implications for catalyst designs and reaction mechanisms. Herein, we report facile C<sub>carbene</sub>-halogen reductive eliminations from NHC copper halide complexes at RT under oxidative conditions. Density functional calculations on a simplified model system suggest that the reactions occur through oxidation of Cu(I) to Cu(III) species followed by C<sub>carbene</sub>-halogen reductive eliminations from NHC Cu(III) halide complexes. Remarkably short C<sub>carbene</sub>-chloride contacts and rare interactions between the chloride lone pair electrons and the C<sub>carbene</sub> p<sub>π</sub> orbital were found for the calculated NHC Cu(III) chlorides. The facile C<sub>carbene</sub>-X reductive elimination reported here warrants consideration as a potential decomposition pathway in reactions involving NHC-supported high-valent metal complexes, especially with late transition metals.

N-heterocyclic carbene (NHC) metal complexes are used widely as catalysts in organic reactions.<sup>1</sup> Compared to other neutral type ligands, NHCs usually form stronger bonds with metals due to excellent  $\sigma$  donating ability. The conjugation between the carbene carbon (C<sub>carbene</sub>) p<sub>π</sub> orbital and nitrogen lone pair electrons in the heterocycle further stabilizes the metal-C<sub>carbene</sub> bonds. As a result, NHCs are often better at suppressing catalyst decompositions. The metal-C<sub>carbene</sub> bonds are remarkably inert compared to other metal-carbon bonds at catalytic metal centers, which are prone to undergo various reactions such as migratory insertion and olefin metathesis.<sup>1</sup> In contrast, only a small number of elementary organometallic reactions, mostly limited to C<sub>carbene</sub>-C reductive elimination and ligand dissociation/displacement, are documented with the metal-C<sub>carbene</sub> bonds.<sup>2-4</sup>

Carbon-halogen (C-X) reductive elimination of metal-C<sub>alkyl</sub> or metal-C<sub>aryl</sub> bonds is an important elementary organometallic reaction,<sup>5</sup> but no well-defined example is reported for C<sub>carbene</sub>-X reductive elimination from NHC metal halide complexes,<sup>6</sup> although such complexes are ubiquitous in NHC chemistry.<sup>1</sup> Herein, we report facile formation of 2-haloimidazoliums from NHC Cu(I) halide complexes at room temperature (RT) under oxidative conditions as well as computational evidence to support a mechanism involving C<sub>carbene</sub>-X reductive elimination from NHC Cu(III) halide complexes.

As a part of our continuing efforts in the characterization of reactivity of Cu(III) complexes,<sup>7</sup> we postulated that NHC Cu(III) complexes might be isolable because of the relatively inert Cu-C<sub>carbene</sub> bond. In that regard, oxidations of IPrCu<sup>I</sup>Cl (**1**<sub>Cl</sub>, IPr: 1, 3-bis(2, 6-

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Supporting Information Available: Detailed experimental and calculational data. This material is available free of charge at <http://pubs.acs.org>.

diisopropylphenyl)imidazol-2-ylidene) by various oxidants were investigated. No significant reaction was observed between **1<sub>Cl</sub>** and [Ph<sub>2</sub>I]<sup>+</sup>PF<sub>6</sub><sup>-</sup> or [Cp<sub>2</sub>Fe]<sup>+</sup>PF<sub>6</sub><sup>-</sup> (0.64 V vs NHE)<sup>8</sup> in acetonitrile (MeCN). By contrast, mixing **1<sub>Cl</sub>** with Selectfluor<sup>®</sup> (≥ 1.5 eq.) or Cu<sup>II</sup>(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub> (≥ 2.0 eq., 1.30 V vs NHE)<sup>9</sup> in MeCN at RT rapidly and quantitatively forms 2-chloro-imidazolium **2<sub>Cl</sub>** (Scheme 1).<sup>10</sup> Quantitative formation of 2-halo-imidazolium **2<sub>Br</sub>** or **2<sub>I</sub>** was realized for IPrCu<sup>I</sup>Br (**1<sub>Br</sub>**) or IPrCu<sup>I</sup>I (**1<sub>I</sub>**) under similar conditions.<sup>11</sup>

These reactions appear to occur through either an inner- or outer-sphere oxidation followed by C<sub>carbene</sub>-X reductive elimination. An outer-sphere oxidation is supported by the *ca.* 80 % formation of **2<sub>Cl</sub>** by reacting **1<sub>Cl</sub>** with [(1, 10-phenanthroline)<sub>3</sub>Fe<sup>III</sup>]<sup>3+</sup> (≥ 2 eq., 1.22 V vs NHE)<sup>12</sup> in MeCN at RT.<sup>13</sup> However, all these reactions are fast even at low temperatures (t<sub>1/2</sub> ~ seconds at *ca.* -40 °C), and no intermediate species could be detected by UV-Vis spectroscopy on a timescale of seconds.

DFT calculations provide mechanistic insights into the oxidation by Selectfluor<sup>®</sup>. The calculated free-energy profiles corresponding to C<sub>carbene</sub>-X reductive elimination from either a Cu(II) or Cu(III) species using a simplified model system (**3**) are shown in Scheme 2.<sup>14</sup> The oxidation of **3** by Selectfluor<sup>®</sup> to form **5**, a three-coordinate Cu(III) species, is thermodynamically favorable.<sup>15</sup> The Cu(III) species is further stabilized by coordination of an MeCN ligand to form **7**.<sup>16</sup> The activation barrier for C<sub>carbene</sub>-Cl reductive elimination from **7** via **TS<sub>1</sub>** to form 2-chloro-imidazolium **10** is remarkably low at 3.5 kcal mol<sup>-1</sup>.<sup>17</sup> The overall reaction is favorable by -54.2 kcal mol<sup>-1</sup>. Other possible Cu(III) species<sup>18</sup> are less stable than **7** and lead to higher activation barriers. Alternatively, **7** could react with another equivalent of **3** to form Cu(II) intermediates **8** and **9**, the two most stable Cu(II) species.<sup>19</sup> Although no transition state from **9** to **10** could be located (the energy monotonically increases as the C<sub>carbene</sub>-Cl separation shortens.), the lower limit of its activation barrier can be estimated by the corresponding reaction free energy, 44.1 kcal mol<sup>-1</sup>, the least endothermic among various Cu(II) species.<sup>19</sup> Therefore, the calculations on the simplified model system favor a mechanism of C<sub>carbene</sub>-Cl reductive elimination from NHC Cu(III) chloride complexes for the oxidation of **1<sub>Cl</sub>** by Selectfluor<sup>®</sup>.

The thermodynamically unfavorable C<sub>carbene</sub>-Cl reductive elimination from **9** is consistent with isolable NHC Cu(II) chloride complexes.<sup>20</sup> Based on these results, we prefer a mechanism with two sequential inner- or outer-sphere 1e<sup>-</sup> oxidations followed by C<sub>carbene</sub>-Cl reductive elimination from NHC Cu(III) chloride complexes for the reaction with Cu(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>.<sup>21</sup> Although the detailed mechanism is still unclear. Furthermore, the quantitative formation of **2<sub>Cl</sub>** instead of IPrCu(II) chloride complexes from the reaction of **1<sub>Cl</sub>** and Selectfluor<sup>®</sup> suggests that C<sub>carbene</sub>-Cl reductive elimination from IPrCu(III) chloride complexes is much faster than reactions of **1<sub>Cl</sub>** to form IPrCu(II) halide complexes. This reactivity is consistent with the calculated 3.5 kcal mol<sup>-1</sup> activation barrier from **7** to **10**. Such a low barrier is probably a consequence of the electrophilic nature of a Cu(III) center that renders the NHC C<sub>carbene</sub> susceptible to nucleophilic attack, as suggested by the remarkably close C<sub>carbene</sub>-Cl contacts (*ca.* 2.7 Å) in **5** and **7** (Figure 1) as well as the interactions between the chloride lone pair electrons and the C<sub>carbene</sub> p<sub>π</sub> orbital (Figure 2). A similar interaction has been invoked to rationalize the short C<sub>carbene</sub>-Cl contact (*ca.* 2.85 Å) in NHC V<sup>V</sup>(O)Cl<sub>3</sub>.<sup>22</sup> In contrast, no evidence of such an interaction exists for **8** (Figure 1).

In summary, we have demonstrated that C<sub>carbene</sub>-halogen reductive eliminations readily occur from NHC copper halides at RT under oxidative conditions. These reactions provide new examples for the well-known oxidation-induced reductive eliminations. DFT calculations on a simplified model system suggest that the involvement of NHC Cu(III) halides is essential for these reactions and the reductive eliminations might be facilitated by the interaction between C<sub>carbene</sub> and the halogen lone pair. Given the ubiquity of NHC metal

halide complexes, the facile  $C_{\text{carbene}}-X$  reductive elimination reported here warrants consideration as a potential decomposition pathway in reactions involving NHC-supported high-valent metal complexes, especially with late transition metals under oxidative conditions.

## Supplementary Material

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## Acknowledgments

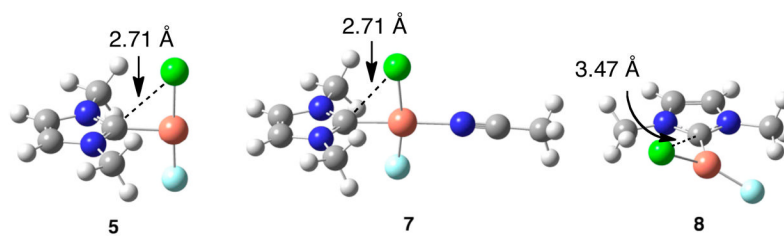
This work was supported by NIH(GM50730) and ACS-PRF award. We thank Dr. Allen G. Oliver for the crystal structures, and Professor Xingwei Li and Dr. George S. Chen for their suggestions in the preparation of the manuscript.

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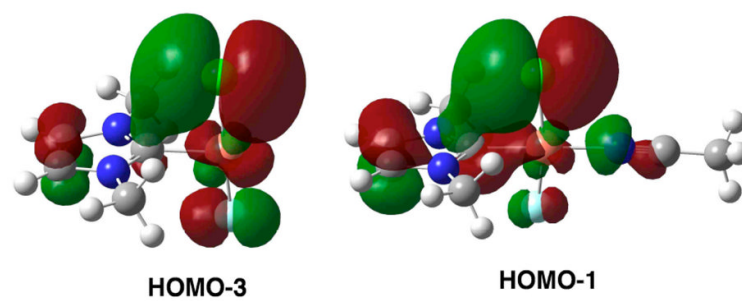
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- Halogenolysis of the metal- $C_{\text{carbene}}$  bonds to form  $C_{\text{carbene}}-X$  bonds does occur, presumably through either direct electrophilic cleavage of metal- $C_{\text{carbene}}$  bonds by  $X_2$  or oxidative addition of  $X_2$  followed by  $C_{\text{carbene}}-X$  reductive elimination. DFT calculations support a direct electrophilic cleavage of Pd- $C_{\text{carbene}}$  bond by  $I_2$ .<sup>9f</sup>(a) Lappert MF, Pye PL. *J Chem Soc, Dalton Trans* 1977:1283–1291. (b) Liu ST, Ku RZ, Liu CY, Kiang FM. *J Organomet Chem* 1997;543:249–250. (c) Cole ML, Davies AJ, Jones C. *J Chem Soc, Dalton Trans* 2001:2451–2452. (d) Fooladi E, Dalhus B, Tilsted M. *Dalton Trans* 2004:3909–3917. [PubMed: 15540136] (e) Heckenroth M, Neels A, Garnier MG, Aebi P, Ehlers AW, Albercht M. *Chem Eur J* 2009;15:9375–9386. (f) Lee, E. Ph D Dissertation. Stanford University; Stanford, CA: 2009.

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10. **2C<sub>1</sub>** was characterized by NMR (<sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F), mass spectroscopy, and X-ray crystallography (**2C<sub>1</sub>**·SbF<sub>6</sub>·CH<sub>2</sub>Cl<sub>2</sub>).<sup>19</sup> Reactions with lesser amounts of oxidants led to unreacted **1C<sub>1</sub>** and lower yields of **2C<sub>1</sub>**. The amounts of oxidant and the color of the reaction solution suggest that the side product is Cu(II) (blue) and Cu(I) (colorless) species for the reaction with Selectfluor<sup>®</sup> and Cu<sup>II</sup>(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>, respectively.
11. **2B<sub>r</sub>** and **2I** were characterized by NMR (<sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F), mass spectroscopy, and X-ray crystallography (**2B<sub>r</sub>**·CF<sub>3</sub>SO<sub>3</sub>·CH<sub>2</sub>Cl<sub>2</sub> and **2I**·**I<sub>3</sub>**).<sup>19</sup> The reaction of IPrCu<sup>I</sup>F with Cu<sup>II</sup>(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub> led to the formation of IPrCu<sup>I</sup>(CF<sub>3</sub>SO<sub>3</sub>) (a crystal structure was obtained),<sup>19</sup> while the reaction with Selectfluor<sup>®</sup> afforded a species with broad <sup>1</sup>H NMR signals similar to that of a reported NHC-ligated Cu(II) dimer<sup>20b</sup>, suggesting that C-F formation is slower than the comproportionation between Cu(I) and Cu(III).
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13. Protonolysis of the Cu-C<sub>carbene</sub> bond was also observed, leading to *ca.* 20 % yield of the corresponding imidazolium. In addition, no well-defined oxidation occurs with **1C<sub>1</sub>** by cyclic voltammetry at low temperatures (*ca.* –40 °C).
14. All calculations were performed at the level of B3LYP/6-311+G\*\* by Gaussian 03 program. The solvation effect was estimated by PCM/UA0 model. Relative free energies are used in the computational discussion. See supporting information for more detailed descriptions of the computational methods. (a) Pople, J. A. et al. Gaussian03, Revision E.01, Gaussian, Inc., Wallingford, CT, 2004. (b) The gas phase entropies were converted to corresponding entropies<sup>19</sup> (1 M in CH<sub>3</sub>CN) according to the method in Wertz DH. *J Am Chem Soc* 1980;102:5316–5322.
15. A 12.8 kcal mol<sup>-1</sup> activation free energy was calculated for this step (fluorine transfer) at a lowerlevel method (B3LYP/6-311+G\*\*//B3LYP/LANL2DZ).<sup>19</sup>
16. **6** is proposed as an intermediate in the reaction. It might ligate to copper in the final uncharacterized Cu(II) product. Coordination of MeCN to **3** might facilitate the oxidation. However, the corresponding 3-coordinate species could not be located computationally.
17. η<sup>2</sup>-Arene-coordination intermediates have been reported in a related computational study for oxidative addition of Ph–Br to various Cu<sup>I</sup> species. (Zhang SL, Liu L, Fu Y, Guo QX. *Organometallics* 2007;26:4546–4554.) By contrast, no analogous intermediate was located computationally for our system.
18. These include two isomers of **7**, one 5-coordinate Cu(III) species, and a complex with **6** coordinated to **5**.<sup>19</sup>
19. See supporting information.
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21. Previous work indicated that AgSbF<sub>6</sub> (1.35 V vs NHE)<sup>8</sup> can oxidize Cu<sup>II</sup>-Salen to [Cu<sup>III</sup>Salen] (SbF<sub>6</sub>) in CH<sub>2</sub>Cl<sub>2</sub>.<sup>7d</sup> Therefore, the oxidation of **1C<sub>1</sub>** to Cu(III) by Cu<sup>II</sup>(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub> (1.30 V vs NHE)<sup>9</sup> seems possible.

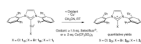
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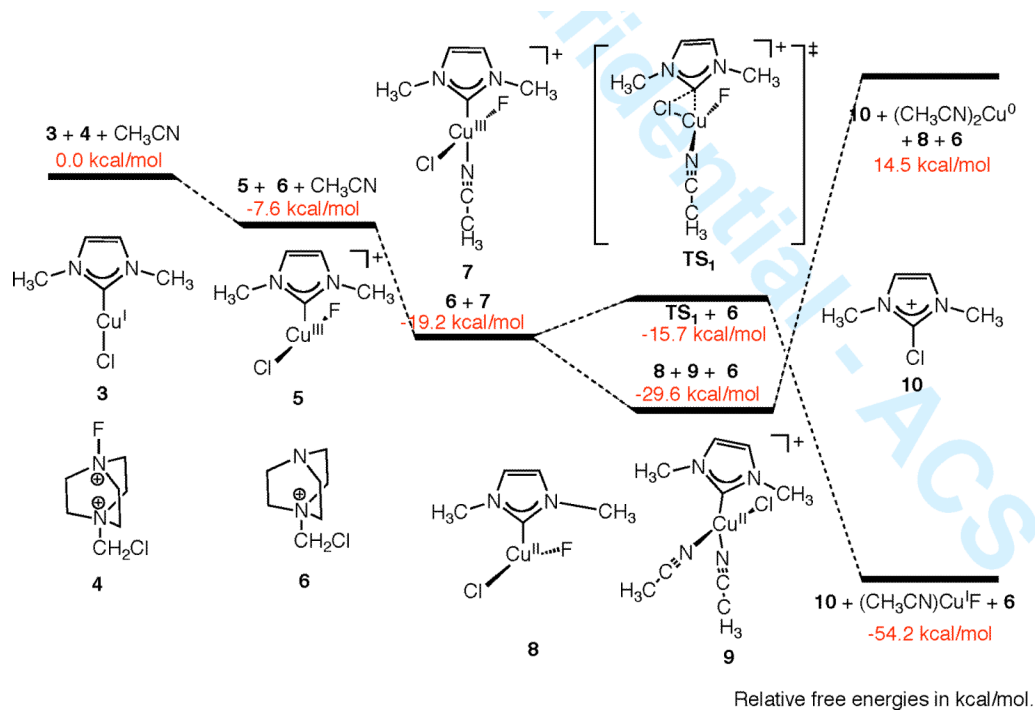
**Figure 1.**  
Optimized structures of **5**, **7**, and **8**.



**Figure 2.**  
HOMO-3 of **5** and HOMO-1 of **7**.

**Scheme 1.**





Scheme 2.